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CABA,
CANCERLIT, CAPLUS, CEABA, CEN, CIN, CONFSCI, CROPB, CROPU, DDFB, DDFU,
DGENE, DRUGB, DRUGLAUNCH, DRUGMENOG2, ...' ENTERED AT 12:39:40 ON 21 SEP
2000

SEA URIDINE(W)PHOSPHOGALACTOSE OR UDP-GALACTOSE

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22 FILE WILDS
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L1 QUE URIDINE W) PHOSPHOGALACTOSE OR UDP-GALACTOSE

FILE 'MEDLINE, EMBASE, SCISEARCH, BIOSIS, CAPLUS, TOXLIT, CANCERLIT'
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L2 2713 S L1 AND SYNTHESIS OR BIOSYNTHESIS OR PROCESS OR PRODUCT
L3 13 S L2 AND MORYNEBACTERIUM
L4 6 DUP REM L3 (9 DUPLICATES REMOVED)

LA ANSWER 1 OF 6 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1000:51636 CAPLUS

DOCUMENT NUMBER: 133:3068

TITLE: New fast enzymatic biosynthesis of oligosaccharides

INVENTOR(S): Defrees, Shawn; Johnson, Karl

PATENT ASSIGNEE(S): Neose Technologies, Inc., USA

SOURCE: FET Int. Appl., 193 pp.

CODEN: RINKE2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2000/09603 | A2 | 20000525 | WO 1999-US27599 | 19991118 |

W: AE, AL, AM, AT, AU, AV, BA, BB, BG, BF, BY, CA, CH, CN, CR, CU,
 CC, CE, DE, DM, EE, EF, FI, GB, GD, GE, GH, GM, HP, HU, ID, IL,
 IN, IS, JP, KE, KG, KP, KR, KS, LC, LK, LR, LS, LT, LU, LV, MA,
 MD, MG, MK, MN, MW, MX, NF, NG, NL, PL, PT, RO, RU, SE, SG, SI,
 SK, SL, TD, TM, TR, TT, TG, UA, US, VE, VN, YU, ZA, ZW, AM,

FW: GH, GM, GE, LS, NW, SD, SL, SE, TE, UG, UW, AT, BE, CH, CY, DE,
DK, ES, FI, FR, GP, GR, IE, IT, LD, ME, NL, PT, SE, BF, BJ, CF,
CG, CI, CM, CA, GD, GW, ML, MR, NE, SN, TD, TG

PFICRITY AFFILN. INFO.: US 1993-109031 19981118

US 1993-1996 19981119

AE This invention provides recombinant cells, reaction mixts., and methods for the enzymic **synthesis** of saccharides. The recombinant cells contain a heterologous gene that encodes a glycosyltransferase which catalyses at least one step of the enzymic **synthesis**, as well a system for generating a nucleotide sugar that can serve as a substrate for

the glycosyltransferase. The nucleotide sugar may be supplied or synthesized by an enzymic pathway comprising a sugar nucleotide regeneration cycle. The reaction mixt. may contain a second cell type **producing** a nucleotide as a substrate for the sugar nucleotide regeneration cycle, preferably by a nucleotide synthase gene. Use of fusion proteins of glycosyltransferase and nucleotide sugar synthase combined with the use of an enzyme for substrate sugar **synthesis** is described. Chem. or enzymic sulfation may be used for the **synthesis** of sulfated sugars. The recombinant cells, reaction mixts., and methods are useful for efficiently synthesizing a large variety of saccharides, including polysaccharides, oligosaccharides, glycoproteins and glycolipids, using relatively low-cost starting materials. **Synthesis** of 2'-sialyllactose using *E. coli* expressing a CMP-sialic acid synthetase/ α .2,3-sialyltransferase fusion protein is described. Optional use of bakers yeast to **produce** CTP used in the sialic acid cycle and substrate for CMP-sialic acid synthase is also described. **Synthesis** of 2'-sialyllactose using *E. coli* expressing a CMP-sialic acid synthetase/ α .2,3-sialyltransferase fusion protein, GlcNAc 2'-epimerase, and sialic acid aldolase to synthesize CMP-sialic acid from GlcNAc is also described. Variations of the method using **Corynebacterium** expressing a CMP-sialic acid synthetase/ α .2,3-sialyltransferase

fusion protein and GTP-synthetase to **produce** the nucleotide, nucleotide sugar, catalyzing sugar transfer to acceptor saccharide is described. Finally, **synthesis** of trisaccharide Gal.alpha.1,3Gal.beta.1,4GlcNAc using **Corynebacterium** expressing UDP-glucose pyrophosphorylase, UDP-glucose-4'-epimerase, .beta.1,4-galactosyltransferase, and .alpha.1,3-galactosyltransferase is described.

L4 ANSWER 2 OF 6 SINCERELY COPYRIGHT 2000 ISI (R)

ACCESSION NUMBER: 1999-49-401 SCISEARCH

THE GENUINE ARTICLE: 443E

TITLE: Cloning and expression of beta 1,4-galactosyltransferase gene from *Helicobacter pylori*

AUTHOR: Endo T (Reprint); Kozumi S; Takata K; Ozaki A

CORPORATE SOURCE: KYOWA HAKKO KOGYO CO LTD, TOKYO RES LABS, 3-6-6 ASAHI KACHI, TOKYO 1448533, JAPAN (Reprint)

COUNTRY OF AUTHOR: JAPAN

SOURCE: GLYCOBIOLOGY, (AUG 2000) Vol. 10, No. 8, pp. 809-813. Publisher: OXFORD UNIV PRESS, GREAT CLAPENDON ST, OXFORD OX2 6DP, ENGLAND. ISSN: 0950-6658.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 1

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB *Helicobacter pylori*, which is a human pathogen associated with gastric and duodenal ulcer, has been shown to express human oncofetal antigens Lewis X and Lewis Y. Although the mammalian glycosyltransferases that synthesize these structures are well characterized, little is known about the corresponding bacterial enzymes. We report that a novel beta 1,4-galactosyltransferase gene (HpgalT) involved in the **biosynthesis** of lipopolysaccharides in *H.pylori* has been cloned and expressed in *Escherichia coli*. The deduced amino acid sequence of the protein (HpGal-T) encoded by HpgalT consists of 274 residues with the calculated molecular mass of 31,751 Da, which does not show significant similarity to those of beta 1,4-galactosyltransferases from mammalian sources and *Neisseria*. It was confirmed that HpGal-T catalyzed the introduction of galactose from UDP-Gal in a beta 1,4 linkage to

accepting

N-acetylglucosamine (GlcNAc) residues by means of high-performance anion-exchange chromatography with pulsed amperometric detection (HPAEC-PAD). When the *E.coli* cells which overexpressed HpgalT was coupled with the UDP-Gal **production** system, which consisted of recombinant *E.coli* cells overexpressing its UDP-Gal **biosynthetic** genes and **Corynebacterium ammoniagenes**, N-acetylglucosamine, a core structure of lipopolysaccharide of *H.pylori*, was efficiently **produced** from ornithine, galactose, and GlcNAc.

L4 ANSWER 3 OF 6 MEDLINE

ACCESSION NUMBER: 1999-49-401 MEDLINE

DOCUMENT NUMBER: 9994-001

TITLE: Large-scale **production** of N-acetylglucosamine through bacterial coupling.

AUTHOR: Endo T; Kozumi S; Takata K; Kakita S; Ozaki A

CORPORATE SOURCE: Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd., Japan.. enido.tetsuo@kyowa.co.jp

SOURCE: CARBOHYDRATE RESEARCH, (1999 Mar 31) 316 (1-4) 179-83. Journal code: CNY. ISSN: 0008-6215.

PUB. COUNTRY: Netherlands

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199-12

ENTRY WEEK: 19991202

AB A large-scale **production** system of N-acetylglucosamine, a core structure of various oligosaccharides, was established by a whole-cell reaction through the combination of recombinant *Escherichia coli* strains and *Corynebacterium ammoniagenes*. Two recombinant *E. coli* strain over-expressed the UDP-Gal **biosynthetic** genes and the beta-(1->24)-galactosyltransferase gene of *Neisseria gonorrhoeae*, respectively. *C. ammoniagenes* contributed the **production** of UTP from orotic acid. N-Acetylglucosamine was accumulated at 279 mM (107 g L⁻¹) after a 38 h reaction (2.5 L in volume) starting from orotic acid, D-galactose, and 2-acetanido-2-deoxy-D-glucose.

L4 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1998:197631 CAPLUS

DOCUMENT NUMBER: 123:256412

TITLE: **Processes for producing sugar nucleotides and complex carbohydrates**

INVENTOR(S): Koizumi, Satoshi; Sasaki, Katsutoshi; Endo, Tetsuo; Tabata, Kazuhiko; Ozaki, Akio

PATENT ASSIGNEE(S): Kyowa Hakko Kogyo Co., Ltd., Japan; Koizumi, Satoshi; Sasaki, Katsutoshi; Endo, Tetsuo; Tabata, Kazuhiko; Ozaki, Akio

SOURCE: ECT Int. Appl., 119 pp.

CODEN: PIXXDL

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9611343 | A1 | 19960316 | WO 1997-JP3226 | 19970312 |
| W: AU, BG, BR, CA, CN, CZ, DE, DK, JP, KR, MX, NO, NZ, PL, RO, SG, SI, SK, UA, US, VN, AM, AQ, BY, EG, KE, MD, RU, TJ, TM | | | | |
| EW: AT, BE, CH, SE, FR, ES, FI, GR, GB, IE, IT, LI, MC, NL, PT, SE | | | | |
| CA 2037849 | AA | 19960401 | CA 1997-1137549 | 19970312 |
| AU 9742263 | A1 | 19960414 | AP 1997-42263 | 19970312 |
| EP 870841 | A1 | 19961014 | EP 1997-440861 | 19970312 |
| E: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| CN 1017185 | A | 19990103 | CN 1997-191696 | 19970317 |
| PRIORITY APPL. INFO.: | | | | |
| | | | JP 1996-144451 | 19960317 |
| | | | JP 1996-185666 | 19961028 |
| | | | WO 1997-JP3226 | 19970312 |

AB Sugar nucleotides are manufd. with microorganism or enzyme **producing** NTP from nucleotide precursor and with microorganism or enzyme **producing** sugar nucleotides from sugar and NTP. Complex carbohydrates are manufd. with the described microorganism/enzyme and microorganism/enzyme that **produces** complex carbohydrates from sugar nucleotide and complex carbohydrate precursor. Also given was **prodn.** of N-acetylglucosamine-1-phosphate with galactokinase-high microorganism.

L4 ANSWER 1 OF 6 MEDLINE

DUPLICATE 1

ACCESSION NUMBER: 1998414050 MEDLINE

DOCUMENT NUMBER: 96414050

TITLE: Large-scale **production** of UDP-**galactose** and glucofructose by coupling metabolically engineered bacteria.

AUTHOR: Koizumi S; Endo T; Tabata K; Ozaki A

CORPORATE SOURCE: Tokyo Research Laboratories, Kyowa Hakko Kogyo Co., Ltd., Machida, Japan.. skoizumi@kyowa.co.jp

SOURCE: NATURE BIOTECHNOLOGY, (1998 Sep; 16 (9): 847-50. Journal code: CQ3. ISSN: 1087-0156.

PUB. COUNTRY: United States
(Journal; Article; JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199901
ENTRY WEEK: 19990104

AB A large-scale **production** system of uridine 5'-diphospho-galactose (UDP-Gal) has been established by the combination of recombinant

Escherichia coli and *Corynebacterium ammoniagenes*. Recombinant *E. coli* that overexpress the UDP-Gal **biosynthetic** genes *galT*, *galK*, and *galU* were generated. *C. ammoniagenes* contribute the **production** of uridine triphosphate (UTP), a substrate for UDP-Gal **biosynthesis**, from orotic acid, an inexpensive precursor of UTP. UDP-Gal accumulated to 72 mM (44 g/L) after a 21 h reaction starting with orotic acid and galactose. When *E. coli* cells that expressed the α gal,4-galactosyltransferase gene of *Neisseria gonorrhoeae* were coupled with this UDP-Gal **production** system, 372 mM (188 g/L) globotriose (Gal α 1gal,4Gal β tal-4Glc), a trisaccharide portion of verotoxin receptor, was **produced** after a 36 h reaction starting with orotic acid, galactose, and lactose. No oligosaccharide by-**products** were observed in the reaction mixture. The **production** of globotriose was several times higher than that of UDP-Gal. The strategy of **producing** sugar nucleotides by combining metabolically engineered recombinant *E. coli* with a nucleoside 5'-triphosphate **producing** microorganism, and the concept of **producing** oligosaccharides by coupling sugar nucleotide **production** systems with glycosyltransferases, can be applied to the manufacture of other sugar nucleotides and oligosaccharides.

L4 ANSWER 6 OF 6 MELLINE DUPLICATE 1
ACCESSION NUMBER: 9718090A MELLINE
DOCUMENT NUMBER: 9718090P
TITLE: The *galE* gene encoding the UDP-galactose 4-epimerase of *Brevibacterium lactofermentum* is coupled transcriptionally to the *dmdF* gene.
AUTHOR: Quirica J A; Marcos A T; Malumbres M; Martin J F
CORPORATE SOURCE: Department of Ecology, Genetics and Microbiology, Faculty of Biology, University of Lein, Spain.
SOURCE: GENE, (1998 Oct 14) 177 (1-2) 103-7.
JOURNAL CODE: EMBL ISSN: 0378-1119.
PUB. COUNTRY: Netherlands
JOURNAL: Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-242413
ENTRY MONTH: 199701

AB The *galE* gene of *Brevibacterium lactofermentum*, encoding UDP-galactose 4-epimerase (EC 5.1.3.2), has been identified by DNA sequencing downstream from the *orf1-sigB-dmdF* region. The arrangement of the *sigB-dtxE-galE* cluster is also conserved in *Corynebacterium diphtheriae*. The deduced *galE* **product** was a protein of 329 aa residues (35.4 kDa) that shared a high degree of identity to known UDP-galactose 4-epimerase proteins from Gram-positive microorganisms (*Streptomyces lividans* and *Streptococcus thermophilus*). Transcriptional analysis of the *dmdF* and *galE* genes in nutrient-rich medium showed that these genes are part of an operon, that is actively transcribed as a bicistronic mRNA during the exponential growth phase, but transcription of the operon is decreased during the stationary growth phase. In addition, the *dmdF* gene was also expressed as a monocistronic 0.7-kb transcript during the active growth phase.

=> d his

L11 ANSWER 37 OF 42 TOXLIT

ACCESSION NUMBER: 1990:98326 TOXLIT

DOCUMENT NUMBER: CA-113-206233P

TITLE: Cloning and expression of **cDNA** for human
membrane-bound beta-1,4-**galactosyltransferase**.

AUTHOR: Fukuda MN; Appert HA

SOURCE: (1990). PCT Int. Appl. PATENT NO. 90 07000 06/28/90 (La
Jolla Cancer Research Foundation).

FUB. COUNTRY: United States

DOCUMENT TYPE: Patent

FILE SEGMENT: CA

LANGUAGE: English

OTHER SOURCE: CA 113:206233

ENTRY MONTH: 199012

AB A full-length **cDNA** encoding the membrane-bound form of beta-1,4-**galactosyltransferase** from human Golgi bodies is cloned and expressed in *Escherichia coli* and antibodies raised to peptides from the protein. The enzyme is involved in post-translational modification of proteins and there are pathol. consequences from deficiencies in the enzyme (congenital dyserythropoietic anemia type II). The full-length **cDNA** was constructed from a pair of overlapping clones from a human placental **cDNA** library in λ dagt11 and expressed in *E. coli* using pIN-III-ompA3 as the expression vector. Antibodies to a peptide from the carboxy-terminal region of the protein were raised in rabbits by conventional methods.

L11 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1991:1540 CAPLUS

DOCUMENT NUMBER: 114:1540

TITLE: Sequence of a **cdna** encoding human
galactose-1-phosphate uridyl transferase

AUTHOR(S): Flach, James E.; Reichardt, Juergen K. V.; Elsas,
Louis J., II

CORPORATE SOURCE: Dep. Pediatr., Emory Univ., Atlanta, GA, 30322, USA

SOURCE: Mol. Biol. Med. (1990), 7(4), 365-9

CODEN: MBIMDG; ISSN: 0735-1313

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A revised sequence of a **cdna** that encodes a human
galactose-1-phosphate uridyl transferase is reported here. The
cdna is 1295 bases in length and encodes a 43,000 Mr protein. The
sequence was derived from a **cdna** clone isolated from a
transformed human lymphoblast cell line and amplified in a polymerase
chain reaction. The revised sequence reveals a higher degree of amino
acid conservation between the human enzyme and the homologous enzymes

from
Escherichia **coli** and yeast than was previously thought to exist.

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| USPT,JPAB,EPAB,DWPI | L11 and Corynebacterium | 2 | L12 |
| USPT,JPAB,EPAB,DWPI | L4 and galactose | 87 | L11 |
| USPT | 4296203.pn. | 1 | L10 |
| USPT | 5516665.pn. | 1 | L9 |
| USPT | 5409817.pn. | 1 | L8 |
| USPT,JPAB,EPAB,DWPI | L5 and orotic acid | 0 | L7 |
| USPT,JPAB,EPAB,DWPI | L2 and orotic acid | 1 | L6 |
| USPT,JPAB,EPAB,DWPI | L2 and galactose | 67 | L5 |
| USPT,JPAB,EPAB,DWPI | L1 and orotic adj acid | 378 | L4 |
| USPT,JPAB,EPAB,DWPI | L1 and orotic adj acid | 378 | L3 |
| USPT,JPAB,EPAB,DWPI | L1 and (sugar adj nucleotide) | 185 | L2 |
| USPT,JPAB,EPAB,DWPI | synthesis OR biosynthesis OR product? Or process? same (sugar adj nucleotide) | 925064 | L1 |

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| USPT,JPAB,EPAB,DWPI | synthesis OR biosynthesis same l3 | 252198 | L5 |
| USPT,JPAB,EPAB,DWPI | (Prepara? OR Process or making or manufacture) same l3 | 7 | L4 |
| USPT,JPAB,EPAB,DWPI | UDP-galactose | 121 | L3 |
| USPT,JPAB,EPAB,DWPI | phosphogalactose | 4 | L2 |
| USPT,JPAB,EPAB,DWPI | (uridine adj phosphogalactose) OR (Uridine adj phosphoglucose) | 0 | L1 |